MRC Clinical Trials Unit

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Introduction to Statistical Analysis Plans for Clinical Trials (SAPs)

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What is a SAP?

"A detailed and technical description of the principal features of the analysis outlined in the protocol".

In other words:

- **A clear description of how the statisticians plan to look at and analyse the data during and at the end of the trial.**
- **A list of what they plan to include in the clinical study report/end of trial report (and subsequently the main results publication).**

Why do we have them?

Important for:	Reduces risk of:
Transparency	Outcome reporting bias (researchers only reporting the ‘interesting’ results)
Reproducibility	Data-driven results (researchers doing many many analysis and presenting only ‘interesting’ findings
Expanding on detail in protocol	

How are SAPs developed? (1)

Starts in the protocol:

“the principal features of the eventual statistical analysis of the data should be described in the statistical section of the protocol” ICH E9

(called v0.01 of the SAP)

How are SAPs developed (2)

- Separate document to the protocol
- Written after protocol finalised
- Completed prior to data analysis and before anyone is unblinded to treatment (if blinded) at the end of the trial
- Usually written by statistician alongside principal investigator
- Reviewed by other statisticians

Ideally written soon after or as the trial starts and before the first interim analysis

What is in a SAP?

- Title and trial registration details
- Introduction
- Study methods
  - Design
  - Randomisation
  - sample size
  - interim stopping guidelines
- Statistical principles
- Trial population
- Analysis

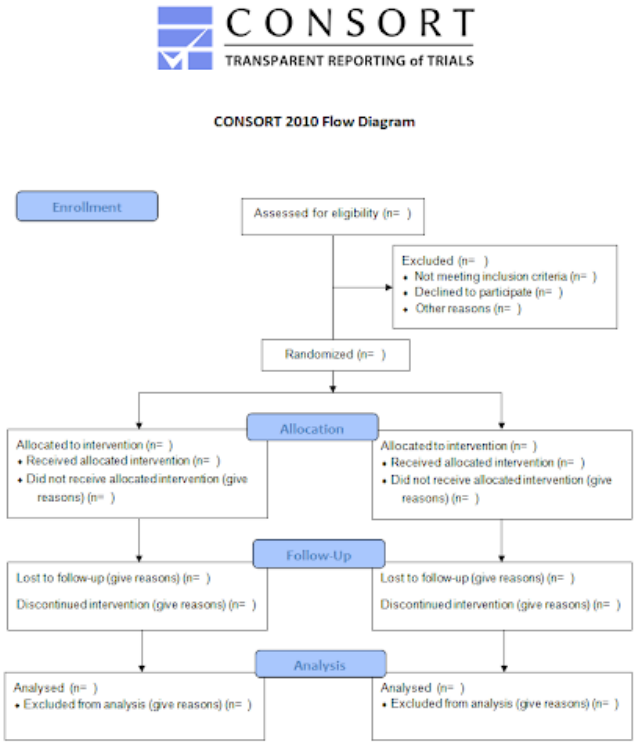
Sections taken from: Gamble C, Krishan A, Stocken D, et al. Guidelines for the Content of Statistical Analysis Plans in Clinical Trials. *JAMA.* 2017;318(23):2337–2343. doi:10.1001/jama.2017.18556

Statistical principles

- How adherence to intervention will be assessed and described
- Definition and description of any protocol deviations
- Definition of analysis populations
  - Are they going to use all those who took the treatment as directed (per protocol)?
  - OR all those randomised regardless of what ended up happening (intention-to-treat)

Trial populations

- Recruitment
- Eligibility summary
- Withdrawals, completion of follow up
- Baseline characteristics
  - How are they going to describe who is in the trial



Analysis

- How exactly are they going to define outcomes
  - Timings, measurements and units, calculations or transformations used
- What analysis method will be used
  - Planned sensitivity analyses (helps check assumptions)
  - Planned subgroup analyses (is the intervention effect different between certain groups of patients)

Peto, R. Current misconception 3: that subgroup-specific trial mortality results often provide a good basis for individualising patient care
Br J Cancer. 2011 Mar 29; 104(7): 1057–1058.

Analysis

- Missing data
  - How do they plan to handle it, what methods will be used
- Additional analyses
  - Anything else that they think they will do which can pre-specified.

Who sees SAPs?

- Trial Management group
  - (which may have PPI representative)
- Trial Steering Committee
  - (which may have PPI representative)
- Data Monitoring Committee
  - (which may have PPI representative)
- Other researchers if protocol is published (SAP is often an appendix)

PPI input in SAP

- May have inputted via protocol through choice of outcomes which links to analysis
- Could be asked to review as part of TMG, TSC or DMC
- Good to check that you feel:
  - Population to be analysed is representative
  - Order of outcomes (primary, secondary etc) is appropriate
  - Includes all important outcomes to you
  - Reflects any developments in research outside of trial
  - Any particular groups of people within the trial that you feel are important to look at separately

Questions and Discussion